REMARKS

Claims 1 – 15 and 19 – 21 are currently pending, with Claims 14,15, and 21 having been withdrawn from consideration. Claims 1, 19, and 20 are the pending independent claims. In the Office Action, , Claims 1 – 13 were rejected as allegedly anticipated by US Patent No. 4,992,419 to Woog et al. ("Woog"). In addition, Claims 19 and 20 were rejected as allegedly obvious over Woog combined with US Patent No. 4,647,454 to Cymbalista.[1]

Each of the foregoing rejections is respectfully traversed. Favorable reconsideration is requested in view of the above amendments and following remarks.

I. Claims 1 – 13.

The Examiner continues to improperly reject Claim 1 and its dependent claims as being anticipated by Woog. As the Applicants have pointed out before, Claim 1 is written in a partially-closed "consisting essentially of" format. Claim 1 is directed to a stable pharmaceutical composition of erythropoietin (EPO) which consists essentially of (1) a therapeutically effective amount of EPO, (2) a pharmaceutically acceptable pH buffering system, (3) polyvinylpyrrolidone (PVP), (4) optionally, an isotonifying agent, (5) optionally, one or more pharmaceutically acceptable excipient(s) selected from the group consisting of polyols, hydroxypropylcellulose, methylcellulose, macrogol esters and ethers, glycol and glycerol esters, and amino acids, and (6) optionally, a poloxamer as an additional stabilizer. Thus Claim 1 excludes additional elements which would materially affect the basic and novel characteristics of the claimed invention. *See Atlas Powder Co. v. E.I. du Pont de Memours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984).

In the Office Action, the Examiner erroneously refuses to give effect to the special "consisting essentially of" transition. She argues that the specification does not

[1] The rejections in the Office Action also refer to Claim 16; however, Claim 16 was cancelled previously and therefore should not have been examined. This is assumed to be an error.

adequately explain what additional components are to be excluded from the composition by the "consisting essentially of" language. However, her argument is unfounded.

While it is true that the specification does not delineate ipis verbis the components that are excluded by the "consisting essentially of" transition, such precision is not necessary. The courts have repeatedly stated that the scope of the term of art "consisting essentially of" claim transition – and the additional components to be excluded therefrom – may be determined from a contextual reading of the specification as a whole. For instance, in *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 68 USPQ2d 1280 (Fed. Cir. 2003), the Federal Circuit interpreted the claim limitation "consisting essentially of aluminum" as permitting only up to about 0.5% silicon in the composition based upon the statement in the applicants' specification that "[s]ilcon contents in the coating metal should not exceed about 0.5% by weight." *See AK Steel*, 344 F.3d at 1240.

Applying this standard to the present case, the Applicants' specification teaches, for example, as follows:

> In the pharmaceutical composition of the present invention, besides the pH buffering system and optionally besides an isotonifying agent and/or a further pharmaceutically acceptable excipient PVP alone may be used as the effective EPO stabiliser and no further stabilisers are necessary for stabilising EPO. PVP can therefore replace the combinations of different stabilisers which are known to be used to maintain the EPO stability in pharmaceutical compositions of EPO described in the prior art.

See, speciation at page 5, last paragraph. In other words, the specification teaches the sufficiency of PVP as the primary, and in many cases the only, EPO stabilizer needed in the claimed composition. In view of this statement in the specification, it is evident that the "consisting essentially of" transition in Claim 1 is adequately elucidated, having been explained as excluding additional EPO stabilizers other then polyvinylpyrrolidone (PVP), and, optionally, a poloxamer stabilizer.

Since Claim 1, as properly interpreted, reads to exclude the use of urea as a stabilizer for EPO, Woog cannot properly be said to anticipate the claim.[2] Woog teaches use urea as the primary stabilizer for EPO. Indeed, Woog states that the addition of urea is "decisive" for the stabilization of EPO.

Only once does Woog appear to disclose an EPO composition without urea. While obviously an error, Example 5 does not list urea. Given Woog's previous insistence that urea is "decisive" for the stabilization of EPO, any person of ordinary skill would conclude that the omission of urea from Example 5 was a mistake or some sort of clerical error.[3] Even if urea was intentionally omitted from Example 5 (which seems exceedingly unlikely), the fact is that Example 5 of Woog does not mention polyvinylpyrrolidone (PVP), the primary stabilizer specified to be "essential" in Applicant's claims. Hence, any way one looks at it, Example 5 of Woog cannot be said to anticipate the subject matter of Claim 1, nor that of its dependent claims.

For at least the above reasons, Woog simply does not anticipate the subject matter of Claim 1 or that of its dependent Claims 3 – 13.

II. Claims 19 and 20.

The Examiner also asserts that Claims 19 and 20 would have been obvious from Woog combined with Cymbalista.

As currently amended, Claim 19 is a "comprising" or open-ended claim which calls for, among other things, a therapeutically effective amount of EPO and an EPO stabilizer. However, Claim 19 is closed with respect to the EPO stabilizer. It requires that the EPO stabilizer consists of polyvinylpyrrolidone (PVP) and, optionally, a

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[2] If urea is "decisive" as a stabilizer for EPO as alleged by Woog, then it would certainly be expected to be excluded (in any significant amount) from Claim 1 of the present application as a material that would affect the "basic and novel characteristics of the claimed composition."

[3] Example 5 is supposed to exemplify the invention as claimed in Woog. If it does, it must have included urea. Also, the math and the results do not appear to be correct unless urea was in fact present in the amount used in the other exemplary claims.

poloxamer. Thus, while the overall claim structure is "open", the claim is "closed" with respect to the use of an EPO stabilizer other than PVP and poloxamer.

Similarly, Claim 20 is an "open" claim calling for erythropoietin (EPO), and polyvinylpyrrolidone (PVP), but the claim also further specifies that the polyvinylpyrrolidone (PVP) is the sole stabilizer for the stabilization of the erythropoietin (EPO).

In view of these limitations, the Examiner' rejections based upon Woog and Cymbalista are also unfounded and not well taken.

As discussed above, Woog teaches a composition in which urea, not PVP, is the principal and "decisive" stabilization agent for EPO. Woog says nothing about PVP, much less PVP and a poloxamer, and therefore can hardly be said to teach use of PVP and a poloxamer as the sole or even the essential stabilizers for EPO in an aqueous solution.

These deficiencies in Woog cannot be cured by resort to Cymbalista. As Applicants have already explained, Cybmalista is directed to the stabilization of interferon β, not EPO. The Examiner has failed to show by any competent evidence that a person of skill would have any reason to assume that a stabilizer effective for one protein would be effective to stabilize a completely different protein.

In fact, persons of skill know very well that internal compatibility vis-à-vis stabilizers and the many thousands of different proteins are not translatable. No one simply assumes a compound effective to stabilize one protein (especially by itself) would be effective to stabilize a chemically different protein. It would be unfounded to do so – Pure speculation! Rejections cannot properly be based on conjectural assumptions with no basis in objective truth or other scientific fact.

Given that Woog believes urea to be critical and decisive for the stabilization of EPO, and that Cymbalista is directed towards the stabilization of interferon β rather than EPO, Cymbalista plainly cannot b said to be suggestive of using PVP to stabilize EPO.

Moreover, Claims 19 and 20 exclude the use of EPO stabilizers other than PVP

and poloxamer (in Claim 19) or PVP alone (in Claim 20). Therefore, the combined teachings of Woog and Cymbalista would not have rendered the subject matter of these claims obvious.

For at least the reasons set forth above, Applicants submit that the obviousness rejection of Claims 19 and 20 based upon the combination of Woog and Cymbalista are not well founded, and should be withdrawn.

In light of the foregoing, the present amendment is believed to place the application in a condition for allowance and entry of the foregoing amendments and allowance of Claims 1 – 15 and 19 – 21 is respectfully solicited.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 12-2355.

Respectfully submitted,
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